

### **REMARKS**

Claims 1 and 3-5 are pending and stand rejected. Claim 3 has been amended with this action. The amendment to claim 3 adds no new matter. Support for the amendment to claim 3 can be found throughout the application, for example at page 4, lines 4-14. The specification has been amended to correct a deficiency in the characterization of an application to which the instant application claims priority. Support for this amendment is inherent to the subject parent application and, accordingly, this amendment adds no new matter.

Applicants gratefully acknowledge the Examiner's withdrawal of prior rejections not specifically reiterated in this Action.

### **Priority**

The Office Action states that the specification's statement of priority "is objected to because it claims only "priority" to PCT/US97/16018, but does not specify what type of priority."

Accordingly, Applicants have amended the priority claim to indicate that the instant application is a continuation of PCT/US97/16017. Reconsideration and withdrawal of the objection is therefore respectfully requested.

### **Double Patenting**

The Office Action states that claims 1, 3 and 4 continue to stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,856,642 for the reasons of record. The Office Action further acknowledges Applicant's commitment to filing a Terminal Disclaimer to the cited patent should any of the currently pending claims be found allowable, and Applicants hereby continue to respectfully request that this rejection be held in abeyance until such time.

### **Rejection under 35 U.S.C. §112, 2nd**

The Office Action states that claim 3 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

which the applicant regards as the invention because “it is unclear how an oligonucleotide can have reduced splenomegaly and reduced depletion of platelets, since these are considered characteristic of whole organisms, and not molecules.”

In response, Applicants respectfully aver that the language of the claimed method, which provides “[a] method for providing a CpG-containing phosphorothioate oligonucleotide with reduced splenomegaly and reduced depletion of platelets to a mammal” (emphasis added), is abundantly clear to the skilled artisan. Nevertheless, in an effort to facilitate prosecution of the application, and not in acquiescence to the rejection, Applicants have amended claim 3 to recite “[a] method for providing a CpG-containing phosphorothioate oligonucleotide with reduced side effects of splenomegaly and depletion of platelets when administered to a mammal...” (emphases added).

Reconsideration and withdrawal of the rejection is therefore respectfully requested.

**Rejection under 35 U.S.C. §102**

The Office Action states that claims 1 and 3-5 have been rejected under 35 U.S.C. §102(b) as being anticipated by Cook (which is U.S. Patent Number 5,212,295). In particular, the Office Action states that “Cook teaches compositions comprising a phosphorothioate oligonucleotide that further comprises a modified CpG motif, wherein said modification is selected from...alkylphosphonate, 2’-O, stereospecific phosphorothioate, phosphotriester, and phosphoramidate CgG motifs,” and further that “[a]lthough Cook does not explicitly teach that such methods would reduce the side effects of the administration of antisense oligos...(nevertheless)...the method of Cook would thus be considered to have the inherent outcome of reducing side effects.” Applicants traverse this rejection for the reasons that follow.

First, Applicants respectfully note that, for a reference to anticipate an invention, each and every element of the claimed invention must be taught by the reference. Applicants respectfully aver that the Cook patent fails to teach the claimed “modified CpG-containing phosphorothioate oligonucleotides” of claim 1, and the associated methods of use of such modified CpG-containing phosphorothioate oligonucleotides of claims 3-5, because this reference fails to specifically teach CpG-containing phosphorothioate oligonucleotides, in

general, as well as the claimed specific modifications to such oligonucleotides, in particular. Indeed, the Cook patent's reference to "CPG" is with regard to "**controlled pore glass (CPG)** supports" which are "standard solid state supports (for oligonucleotide synthesis) known in the art" (see col. 18, lines 65-67). In contrast, Applicants' invention is directed to modified phosphorothioate oligonucleotides that include one or more specific CpG motifs. A CpG motif includes a Cytidine nucleoside linked via a phosphorus linkage to a Guanosine nucleoside. Stated otherwise, Applicants' invention includes phosphorothioate oligonucleotides having specific modifications to one or more CpG dinucleosides.

Nowhere does Cook explicitly teach a CpG-containing phosphorothioate oligonucleotides, let alone the claimed modified CpG-containing phosphorothioate oligonucleotides that provide for reduced immune side-effects when administered to a mammal. The few oligonucleotide sequences provided by Cook, at col. 13, lines 6-15, are neither taught to be phosphorothioate oligonucleotides, nor, more importantly, taught to contain the claimed modifications at one or more of their CpG dinucleoside linkages. Indeed, the teachings of Cook generally instruct the production of chirally pure phosphorothioate or methylphosphonate or phosphotriester or phosphoramidate oligonucleotides, and not the claimed specific combination of racemic phosphorothioate-containing-CpG-linkage modified oligonucleotides of the invention.

Therefore, because Cook does not teach each and every element of the claimed modified oligonucleotides of claim 1, or their associated methods of use as provided in claims 3-5, it does not anticipate Applicants' invention. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

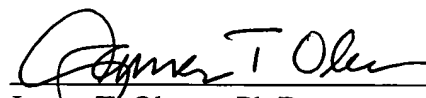
Appln. No. 09/103,745  
Amdt. dated October 26, 2005  
Reply to Office Action of August 24, 2005  
Attorney Docket No.: 047508.642US2 (HYZ-642US2)

### CONCLUSION

In view of the foregoing remarks, Applicants respectfully submit that the pending claims are in condition for allowance. If a telephone interview would advance prosecution of the application, the Examiner is invited to call the undersigned at the number listed below.

This Action is being filed within three months of the mailing date of the last Office Action. Accordingly, no further fees are believed to be due in connection with the filing of this Amendment, however the Commissioner is authorized to debit Deposit Account No. 08-0219 for any required fee necessary to maintain the pendency of this application.

Respectfully submitted,



---

James T. Olesen, Ph.D.  
Attorney for Applicants  
Reg. No. 46, 967

Dated: October 26, 2005

Wilmer Cutler Pickering Hale and Dorr LLP  
60 State Street  
Boston, MA 02109  
617-526-6045 (telephone)  
617-526-5000 (facsimile)